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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,076	03/27/2002	James B. McCarthy	110.01270101	4527

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EXAMINER

HADDAD, MAHER M

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/937,076

Applicant(s)

MCCARTHY ET AL.

Examiner

Maher M. Haddad

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 November 2004 and 22 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-10,13,17-21,25,28,31,32, 35,38 and 41 is/are pending in the application.
- 4a) Of the above claim(s) 1, 4-10, 13, 17-21, 25, 28, 31, 32 and 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38 and 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/8/04 and 12/22/04, is acknowledged.
2. Claims 1, 4-10, 13, 17-21, 25, 28, 31-32, 35, 38 and 41 are pending.
3. Claims 1, 4-10, 13, 17-21, 25, 28, 31, 32 and 35 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
4. Claims 38 and 41 are under consideration in the instant application as they read on a composition comprising a $\beta 1$ integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO: 3) and a pharmaceutically acceptable carrier.
5. Regarding Applicant's comments regarding the restriction requirement, the Examiner's position is that Applicant's inventions do not have a single general inventive concept and so lack unity of invention as set forth in the previous Office Action. The requirement is made FINAL in the previous Office Action mailed 8/10/04.
6. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional applications 60/167,538 and 60/125,634 upon which priority is claimed fails to provide adequate support for SEQ ID NO: 3 of this application. The filing date of the instant applicant is deemed to be 03/22/2000 rather than 03/22/1999 as previously stated.
7. The following new ground of rejection is necessitated by the amendment submitted 11/8/04.
8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brienzo PhD thesis, 1998, (IDS ref) in view of WO 99/37669 (IDS Ref. 11).

Art Unit: 1644

Brienzo tested peptides consisting of single successive amino-terminal amino acid deletions of peptide Fn-C/H V-Y, such as QPPRARIY (see fig 7a, 3rd sequence in particular), for their ability to inhibit Ramos cell adhesion to rCS1. Brienzo teaches that as expected, Fn-C/H V-Y, and not scrambled FN-C/H V-Y, completely inhibits Ramos cell adhesion to rCS1 at 0.42mM (i.e., composition), the highest concentration evaluated (figure 7a, b, and page 77, 1st paragraph in particular).

The claimed invention differs from the Brienzo reference teachings only by the recitation of the alanine knockout analog of Fn-C/H V+Y of a single Arg amino acid.

The '669 publication teaches that it has surprisingly been discovered that the alanine knockout analogs of FN-C/H V+Y which preserve the C-terminal LipAr motif (i.e., retain the C-terminal Ile-Try dipeptide sequence) are capable of inhibiting B1 integrin dependent cell adhesion. Further the '669 publication teaches that the term "alanine knockout analog" refers to an analog of a peptide in which a single residue has been substituted by an alanine residue. Further, two of the alanine knockout analogs of FN-C/H V+Y have an alanine residue substituted for one of the arginine residues in the "PRARI" motif (Pro-Arg-Ala-Arg-Ile) within FN-C/H V+Y which has previously demonstrated to be implicated in stimulated focal contact formation (see page 6, line 27 to page 7, line 4 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to alanine knockout one of the arginine residues in the "PRARI" motif taught by the '669 publication of the QPPRARIY to arrive to the claimed QPPRAAIY analog.

Given that "PRARI" motif (Pro-Arg-Ala-Arg-Ile) within FN-C/H V+Y which is implicated in stimulated focal contact formation and that QPPRARIY has ability to inhibit Ramos cell adhesion to rCS1, one of ordinary skill in the art at the time the invention was made would have been motivated to substitute one of the arginine residues in the "PRARI" motif because such alanine knockout is capable of inhibiting β 1 integrin dependent cell adhesion as taught by the '669 publication.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claims 38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,849,712.

The '712 patent teaches the peptide QPPRARIY (see Fig. 7 in particular) variant, that inhibits inhibit Ramos cell adhesion to IIICS-GST as a function of the concentration (mg/ml) (i.e. composition) of a number of truncated analogs of FN C/H V+Y (see col., 2, lines 45-48 in particular).

Art Unit: 1644

The claimed invention differs from the '712 patent teachings only by the recitation of the alanine knockout analog of FN-C/H V+Y of a single Arg amino acid.

The '712 patent further teaches that it has surprisingly been discovered that the alanine knockout analogs of FN-C/H V+Y which preserve the C-terminal LipAr motif (i.e., retain the C-terminal Ile-Tyr dipeptide sequence) are capable of inhibiting β 1 integrin dependent cell adhesion. Further, the term "alanine knockout analog" refers to an analog of a peptide in which a single residue has been substituted by an alanine residue. Two of the alanine knockout analogs of FN-C/H V+Y have an alanine residue substituted for one of the arginine residues in the "PRARI" motif (Pro-Arg-Ala-Arg-Ile (patented SEQ ID NO:39)) within FN-C/H V+Y which has previously demonstrated to be implicated in stimulated focal contact formation. These alanine knockout analogs have the amino acid sequences WQPPRAAIY (patented SEQ ID NO:8) and WQPPAARIY (patented SEQ ID NO:17) (see col., 4, line 61 to col, 5, line 8 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to alanine knockout one of the arginine residues in the "PRARI" motif taught by the '712 patent of the QPPRARIY to arrive to the claimed QPPRAAIY analog.

Given that **PRARI**" motif (Pro-Arg-Ala-Arg-Ile within FN-C/H V+Y is implicated in stimulated focal contact formation and that peptide **QPPRARIY** inhibits inhibit Ramos cell adhesion to IIICS-GST, one of ordinary skill in the art at the time the invention was made would have been motivated to substitute one of the arginine residues in the "PRARI" motif because such alanine knockout is capable of inhibiting β 1 integrin dependent cell adhesion as taught by the '712 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

Art Unit: 1644

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 13, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner